WEST Search History

DATE: Friday, February 28, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ			
L12	L3 and L6	54	L12
L11	L3 and L5	108	L11
L10	L2 and L6	0	L10
L9	L2 and L5	0	L9
L8	L1 and L6	21	L8
L7	L1 and L5	66	L7
L6	ribozym$3	9962	L6
L5	antisens$3	28519	L5
L4	1, 25 dihydroxyvitamin D3 receptor	0	L4
L3	vitamin D receptor	596	L3
L2	NR1I1	1	L2
L1	VDR	887	L1

END OF SEARCH HISTORY

FILE 'HOME' ENTERED AT 11:41:4[illegible] ON 2[illegible] FEB [illegible]

FILE 'BIOSIS, MEDLINE, CAPLUS, EMBASE, CANCERLIT' ENTERED AT 11:4[illegible]:4[illegible] ON 2[illegible] FEB [illegible]

L1 [illegible] VDR
L2 4 DR[illegible]
L3 [illegible] VITAMIN D RECEPTOR
L4 [illegible] VITAMIN D 1, 25-DIHYDROXYVITAMIN D3 RECEPTOR
L5 [illegible] 1, 25-DIHYDROXYVITAMIN D3 RECEPTOR
L6 [illegible] ANTISERUM
L7 [illegible] RIBOZYM[illegible]
L8 [illegible] L[illegible] AND L7
L9 [illegible] DUP REM L8 ([illegible] DUPLICATES REMOVED)
L10 [illegible] L[illegible] AND L[illegible]
L11 [illegible] L[illegible] AND L[illegible]
L12 [illegible] L[illegible] AND L[illegible]
L13 [illegible] L3 AND L6
L14 41 DUP REM L13 ([illegible] DUPLICATES REMOVED)
L15 4 L3 AND L7
L16 4 DUP REM L15 ([illegible] DUPLICATES REMOVED)
L17 [illegible] L5 AND L6
L18 [illegible] L5 AND L7

L4 ANSWER 1 OF 23 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE

ACCESSION NUMBER: 2003:[illegible] BIOSIS
DOCUMENT NUMBER: PREV200[illegible]
TITLE: Non-genomic stimulation of tyrosine phosphorylation cascades by 1,25-D in muscle cells: **VDR**-dependent and -independent mechanisms.
AUTHOR(S): [illegible]
CORPORATE SOURCE: [illegible]
SOURCE: [illegible]
DOCUMENT TYPE: Article
LANGUAGE: English

AB Studies with different cell types have shown that modulation of Ca2+ as well as long-term responses to 1,25(OH)2D3 depends on the activation of tyrosine kinase pathways. Recent investigations of our laboratory have demonstrated that 1,25(OH)2D3 rapidly stimulates in muscle cells tyrosine phosphorylation of PLC-gamma and the growth-related proteins MAPK and c-myc. We have now obtained evidence using **antisense** technology indicating that **VDR**-dependent activation of Src mediates the fast stimulation of tyrosine phosphorylation of c-myc elicited by the hormone. This non-genomic action of 1,25(OH)2D3 requires tyrosine phosphorylation of the **VDR**. Immunoprecipitation under native conditions coupled to Western blot analysis revealed 1,25(OH)2D3-dependent formation of complexes between Src and the **VDR** and c-myc. However, the activation of MAPK by the hormone was only partially mediated by the **VDR** and required in addition increased PKC and intracellular Ca2+. Following its phosphorylation, MAPK translocates into the nucleus where it regulates c-myc transcription. Altogether these results indicate that tyrosine phosphorylation plays a role in the stimulation of muscle cell growth by 1,25(OH)2D3. Data were also obtained involving tyrosine kinases and the **VDR** in hormone regulation of the Ca2+ messenger system by mediating the stimulation of store-operated calcium (SOC; TRP) channels. Congruent with this action, 1,25(OH)2D3 induces a rapid translocation of the **VDR** to the plasma cell membrane which can be blocked by tyrosine kinase inhibitors. Of mechanistic relevance, an association between the **VDR** and TRP proteins with the participation of the scaffold protein INAD was shown.

L4 ANSWER 2 OF 23 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE

ACCESSION NUMBER: 2002:[illegible] BIOSIS
DOCUMENT NUMBER: PREV20[illegible]
TITLE: Alteration of cellular phosphorylation state affects vitamin D receptor-mediated DNA binding in rat muscle cells.
AUTHOR(S): [illegible]
CORPORATE SOURCE: [illegible]
SOURCE: [illegible]
DOCUMENT TYPE: Article
LANGUAGE: English

AB Expression of the vitamin D receptor (**VDR**) is tightly regulated by 1,25-dihydroxyvitamin D3 (1,25-D). In rat L6 muscle cells, however,

typical vitamin D responsive element has not been found in the 5'-flanking region of the CYP3A4 gene, the mechanism of 1,25(OH)2D3-induced CYP3A4 mRNA expression is poorly understood. In the present study, we demonstrated that vitamin D receptor (**VDR**) is a critical factor for the induction using the **antisense** oligonucleotide technique. In addition, we found that treatment of Caco-2 cells with the protein kinase C (PKC) inhibitors, staurosporine and GF109203X, and the tyrosine kinase inhibitor, genistein, but not with the protein kinase A inhibitor, H-89, suppressed CYP3A4 mRNA induction by 1,25(OH)2D3. The depletion of PKC by prolonged treatment with phorbol ester abolished the induction. On the other hand, protein kinase inhibitors used had no effects on the constitutive expression of **VDR** mRNA. Therefore, these observations suggest that 1,25(OH)2D3-induced CYP3A4 mRNA expression might be involved in phosphorylation events in addition to transcriptional regulation via **VDR**. However, 1,25(OH)2D3 did not rapidly activate PKC in the Caco-2 cells used, while the treatment with staurosporine and GF109203X, but not genistein, decreased basal PKC activity by apprx30% of the controls. Taken together, these findings suggest that the change in the phosphorylation state via PKC and tyrosine kinase might, at least in part, modulate 1,25(OH)2D3-induced CYP3A4 mRNA expression via **VDR**.

L4 ANSWER 3 OF 23 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4

ACCESSION NUMBER: 2002:146644 BIOSIS
DOCUMENT NUMBER: PREV200200146644
TITLE: The vitamin D receptor mediates rapid changes in muscle protein tyrosine phosphorylation induced by 1,25(OH)2D3.
AUTHOR(S): Buitrago, Claudia; Vazquez, Guillermo; De Boland, Ana R.; Boland, Ricardo (1)
CORPORATE SOURCE: (1) Departamento de Biologia, Bioquimica and Farmacia, Universidad Nacional del Sur, San Juan 670, 8000, Bahia Blanca: rboland@criba.edu.ar Argentina
SOURCE: Biochemical and Biophysical Research Communications, (December 21, 2001) Vol. 289, No. 5, pp. 1150-1156. http://www.academicpress.com/bbrc. print. ISSN: 0006-291X.
DOCUMENT TYPE: Article
LANGUAGE: English
AB It has been recently shown that the fast non-genomic responses of 1,25(OH)2-vitamin D3 (1,25(OH)2D3) in skeletal muscle cells involve tyrosine phosphorylation of MAP kinase (ERK1/2), c-Src kinase and the oncoprotein c-myc. In the present work, blockade of vitamin D receptor (**VDR**) expression (approx60%) by preincubation of chick embryonic muscle cells with three different **antisense** oligonucleotides against the **VDR** mRNA (AS-**VDR** ODNs) significantly reduced (-24%) 1,25(OH)2D3 stimulation of c-myc tyrosine phosphorylation and inhibited c-Src tyrosine dephosphorylation implying lack of c-Src activation by the hormone. Co-immunoprecipitation experiments revealed that 1,25-(OH)2D3 induces the formation of complexes between c-Src and c-myc, in agreement with the above results and previous studies showing hormone-dependent association between c-Src and tyrosine phosphorylated **VDR** and c-Src mediated c-myc tyrosine phosphorylation. MAPK tyrosine phosphorylation by 1,25(OH)2D3 was affected to a lesser extent (-35%) by transfection with AS-**VDR** ODNs implying that both **VDR**-dependent and **VDR**-independent signalling mediate hormone stimulation of MAPK. These are the first results providing direct evidence on the participation of the **VDR** in non-genomic 1,25(OH)2D3 signal transduction. Activation of tyrosine phosphorylation cascades through this mechanism may contribute to hormone regulation of muscle growth.

L4 ANSWER 4 OF 23 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE

ACCESSION NUMBER: [illegible]:247104 BIOSIS
DOCUMENT NUMBER: PREV2[illegible]247104
TITLE: Steroid receptor co-activator-1 mediates 1,25-dihydroxyvitamin D3-stimulated alkaline phosphatase in human osteosarcoma cells.
AUTHOR(S): [illegible], R. K. (1); Bell, N. H.
CORPORATE SOURCE: (1) Department of Medicine, Division of Bone and Mineral Metabolism, Medical University of South Carolina, [illegible] [illegible] Street, Charleston, SC, [illegible] USA
SOURCE: Calcified Tissue International, (May, [illegible]) Vol. [illegible], No. [illegible], pp. [illegible].
ISSN: [illegible].
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB For steroid hormone function to occur, nuclear receptors interact with a series of coactivators including steroid receptor coactivator-1 (SRC-1). The SRC-1 binds the vitamin D receptor (**VDR**) in the presence of ligand in an activation function 2 (AF-2)-dependent manner. In order to understand the role of this interaction in 1,25-dihydroxy-vitamin D3 (1,25(OH)2D3)-mediated gene expression, the level of SRC-1 expression was altered in MG-63 cells. Previous studies had demonstrated that MG-63 cells express the **VDR** and that 1,25(OH)2D3 regulates expression of alkaline phosphatase (ALP). Analysis of MG-63 cells demonstrated that SRC-1 is expressed. A full-length cDNA coding for SRC-1 was inserted in **antisense** orientation into an expression vector (anti-SRC-1). The MG-63 cells were transfected with anti-SRC-1 or mock vector and stable transformants were selected. Western blot analysis showed a [illegible] reduction in SRC-1 protein as compared with mock cells. We determined the effect of normal and reduced SRC-1 expression in MG-63 cells on 1,25(OH)2D3-mediated stimulation of ALP. Whereas [illegible] M 1,25(OH)2D3 produced a [illegible]-fold stimulation in ALP in mock cells expressing normal levels of SRC-1, it did not alter ALP in cells expressing reduced levels of SRC-1. Thus, SRC-1 is required for 1,25(OH)2D3-mediated gene expression of ALP by human MG-63 cells.

L9 ANSWER 5 OF 23 BIOSIS COPYRIGHT [illegible] BIOLOGICAL ABSTRACTS INC.DUPLICATE 8
ACCESSION NUMBER: 2000:[illegible] BIOSIS
DOCUMENT NUMBER: PREV2[illegible]
TITLE: 1alpha,25-dihydroxyvitamin D3-induced myeloid cell differentiation is regulated by a vitamin D receptor-phosphatidylinositol 3-kinase signaling complex.
AUTHOR(S): Hmama, Zakaria; Nandan, Devki; Sly, Laura; Knutson, Keith L.; Herrera-Velit, Patricia; Reiner, Neil E. (1)
CORPORATE SOURCE: (1) Division of Infectious Diseases, University of British Columbia, 2733 Heather St., Rm. 452D, Vancouver, BC Canada
SOURCE: Journal of Experimental Medicine, (Dec. [illegible], [illegible]) Vol. [illegible], No. 11, pp. [illegible].
ISSN: [illegible].
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB 1alpha,25-dihydroxyvitamin D3 (D3) promotes the maturation of myeloid cells and surface expression of CD14 and CD11b, markers of cell differentiation [illegible]. To examine how these responses are regulated, THP-1 cells were grown in serum-free medium and incubated with D3. This was associated with rapid and transient increases in phosphatidylinositol 3-kinase (PI 3-kinase) activity. Furthermore, induction of CD14 expression in response to D3 was abrogated by the PI 3-kinase inhibitors LY294002 and wortmannin; by **antisense** oligonucleotides to mRNA for the p110 catalytic subunit of PI 3-kinase; and by a dominant negative mutant of PI 3-kinase. In THP-1 cells, induction of CD11b expression by D3 was also abrogated by LY294002 and

wortmannin. Similarly, LY294002 and wortmannin inhibited D3-induced expression of both CD14 and CD11b in peripheral blood monocytes. In contrast to CD14 and CD11b, hormone-induced expression of the CDK inhibitor p21 in THP-1 cells was unaffected by either wortmannin or LY294002. These findings suggest that PI 3-kinase selectively regulates D3-induced monocyte differentiation, independent of any effects on p21. Pretreatment of THP-1 cells with **antisense** oligonucleotides to the vitamin D receptor (**VDR**) mRNA abrogated both activation of PI 3-kinase in response to D3 and hormone-induced CD14 expression. Moreover, both Western blots and in vitro kinase assays carried out on immunoprecipitates of the **VDR** showed that D3 treatment brought about formation of a complex containing both PI 3-kinase and the **VDR**. These findings reveal a novel, nongenomic mechanism of hormone action regulating monocyte differentiation, in which vitamin D3 activates a **VDR**- and PI 3-kinase-dependent signaling pathway.

L9 ANSWER 6 OF 23 BIOSIS COPYRIGHT [illegible] BIOLOGICAL ABSTRACTS INC.DUPLICATE [illegible]

ACCESSION NUMBER: [illegible] BIOSIS
DOCUMENT NUMBER: PREV[illegible]
TITLE: Characterization of an enhancer required for 1,25-dihydroxyvitamin D3-dependent transactivation of the rat osteocalcin gene.
AUTHOR(S): Sneddon, W. Bruce; Demay, Marie B. (1)
CORPORATE SOURCE: (1) Endocrine Unit Wellman 501, Massachusetts General Hospital, Boston, MA, 02114 USA
SOURCE: Journal of Cellular Biochemistry, (June 1, [illegible]) Vol. [illegible], No. 3, pp. 4[illegible].
ISSN: 0730-2312.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The sequences in the rat osteocalcin gene that lie 3' to the vitamin D response element (VDRE) contain a GGTTTGG motif (-420 to -414) that is essential for transcriptional activation of osteocalcin-CAT (OC-CAT) fusion genes by 1,25(OH)2D3. A second copy of this motif, present on the **antisense** strand is unable to compete for nuclear protein binding to the VDRE-associated motif, suggesting that the core element extends beyond the GGTTTGG motif. In order to examine the base requirements for both function and nuclear protein interactions with the VDRE-associated GGTTTGG enhancer motif, deletion and substitution of flanking sequences was performed in the context of both the native osteocalcin promoter and a heterologous viral promoter. These data demonstrate that the base requirements for protein-DNA interactions and transactivation are located between -430 and -414. The position of the element with respect to the VDRE is flexible and insertion of additional copies either 5' or 3' to the VDRE further enhances transactivation, both in the context of the native osteocalcin promoter and a heterologous viral promoter. These data demonstrate that **VDR**-dependent transactivation of the rat osteocalcin gene requires not only the VDRE (-456 to -440) but also sequences between -430 and -414. The protein(s) that interacts with these sequences is capable of enhancing transcription in both a position- and orientation-independent fashion.

L9 ANSWER 7 OF 23 BIOSIS COPYRIGHT [illegible] BIOLOGICAL ABSTRACTS INC.DUPLICATE [illegible]

ACCESSION NUMBER: [illegible] BIOSIS
DOCUMENT NUMBER: PREV[illegible]
TITLE: [illegible]
AUTHOR(S): [illegible]
CORPORATE SOURCE: [illegible]

Koyakidai, [illegible] City, Saitama [illegible] Japan

SOURCE: Journal of Biological Chemistry, (June 12, [illegible]) Vol. [illegible], No. 24, pp. 147[illegible]-14744.
ISSN: [illegible].

DOCUMENT TYPE: Article

LANGUAGE: English

AB The present study demonstrates 1alpha,25-dihydroxyvitamin D3 (1alpha-25(OH)2D3) synergism with transforming growth factor (TGF)-beta1-induced activator protein-1 (AP-1) activity in [illegible] osteoblastic [illegible] cells via the nuclear receptor of the vitamin. 1alpha-25(OH)2D3 synergistically stimulated TGF-beta1-induced expression of the c-jun gene in the cells [illegible]. We initially showed by a gel mobility shift assay 1alpha-25(OH)2D3 synergism of TGF-beta1-induced AP-1 binding to the 12-O-tetradecanoylphorbol-13-acetate response element (TRE). 1alpha-25(OH)2D3 markedly stimulated the transient activity of TGF-beta1-induced AP-1 in the cells transfected with a TRE-chloramphenicol acetyltransferase (CAT) reporter gene. Also, a synergistic increase in TGF-beta1-induced CAT activity was observed in the cells cotransfected with an expression vector encoding vitamin D receptor (**VDR**) and the reporter gene. However, the synergistic CAT activity was inhibited by pretreatment with **VDR** **antisense** oligonucleotides. In addition, in a Northern blot assay, we observed 1alpha-25(OH)2D3 synergism of TGF-beta1-induced expression of the c-jun gene in the cells transfected with the **VDR** expression vector and also found that the synergistic action was clearly blocked by **VDR antisense** oligonucleotide pretreatment. The present study strongly suggests a novel positive regulation by 1alpha-25(OH)2D3 of TGF-beta1-induced AP-1 activity in osteoblasts via "genomic action."

L4 ANSWER [illegible] OF [illegible] BIOSIS COPYRIGHT [illegible] BIOLOGICAL ABSTRACTS INC. DUPLICATE [illegible]

ACCESSION NUMBER: [illegible] BIOSIS

DOCUMENT NUMBER: PREV[illegible]

TITLE: A negative vitamin D response DNA element in the human parathyroid hormone-related peptide gene binds to vitamin D receptor along with Ku antigen to mediate negative gene regulation by vitamin D.

AUTHOR(S): Nishishita, Toshihide; Okazaki, Tomoki (1); Ishikawa, Toshio; Igarashi, Tetsuya; Hata, Keishi; Ogata, Etsuro; Fujita, Toshiro

CORPORATE SOURCE: (1) Endocrine Genet. Hypertension Unit, 4th Dep. Internal Med., Univ. Tokyo Sch. Med., Bunkyo-ku, Tokyo [illegible] Japan

SOURCE: Journal of Biological Chemistry, (May 1, [illegible]) Vol. [illegible], No. 1[illegible], pp. [illegible].
ISSN: [illegible].

DOCUMENT TYPE: Article

LANGUAGE: English

AB We found that the human parathyroid hormone-related peptide (hPTHrP) gene contained a DNA element (nVDREhPTHrP) homologous to a negative vitamin D response element in the human parathyroid hormone gene. [illegible] vitamin D receptor (**VDR**) [illegible] retinoid X receptor alpha [illegible] (RXRalpha) in the human [illegible] cells. **VDR** binding [illegible] this element was [illegible] assay [illegible] with [illegible] anti-**VDR** [illegible] antibody, and this binding activity was [illegible] by 1,25-dihydroxyvitamin D3 [illegible] repression was [illegible] treatment, [illegible] that 1,25-dihydroxyvitamin D3 [illegible] **VDR** [illegible] binding activity [illegible] nVDREhPTHrP. In [illegible] mobility shift assay, we found anti-Ku antigen antibody [illegible] the Ku nuclear protein-nVDREhPTHrP complex. The nVDREhPTHrP-[illegible] plasmid [illegible] vitamin D-dependent inhibition of the reporter activity in [illegible] cells, which was markedly [illegible] by the [illegible] of the Ku antigen expression vector in the **antisense** orientation. On the other hand, such a procedure did not [illegible] the vitamin D [illegible]

[illegible]-mediated gene stimulation by vitamin D. These results indicate that [illegible] interacts with [illegible] in addition to **VDR** to mediate gene suppression by vitamin D.

L9 ANSWER [illegible] OF [illegible] BIOSIS COPYRIGHT [illegible] BIOLOGICAL ABSTRACTS INC.DUPLICATE [illegible]

ACCESSION NUMBER: [illegible] BIOSIS
DOCUMENT NUMBER: PREV[illegible]
TITLE: **Antisense** inhibition of vitamin D receptor expression induces apoptosis in monoblastoid [illegible] cells.
AUTHOR(S): Hewison, Martin [illegible]; [illegible]rowski, Michal; [illegible], Philip; Faulkner, [illegible]; [illegible]erill, Fi[illegible] [illegible].; Bri[illegible], [illegible]; O'Riordan, Jeffrey L. H.; Katz, David R.
CORPORATE SOURCE: [illegible] Dep. Medicine, Univ. Birmingham, Queen Elizabeth Hosp., Edgbaston, Birmingham B15 2TH UK
SOURCE: Journal of Immunology, [illegible] Vol. [illegible], No. 11, pp. 43[illegible]-44[illegible].
ISSN: [illegible].
DOCUMENT TYPE: Article
LANGUAGE: English
AB The active vitamin D-3 metabolite 1,25-dihydroxyvitamin D-3 (1,25(OH)-2D-3) acts as an antiproliferative and differentiating agent for the monoblastoid cell line U937 and as an important immunologic mediator implicated particularly in the function of cells belonging to the monocyte/macrophage lineage. These effects are controlled by the vitamin D receptor (**VDR**), a member of the steroid hormone receptor family. The objective of this study was to develop U937 transfectants expressing **antisense VDR** mRNA, and to use these to examine the role of 1,25(OH)-2D-3-**VDR** interaction in this lineage. A 2-kb **VDR** cDNA insert (including the complete **VDR** coding region) was cloned in an **antisense** orientation into the EBV episomal vector pMEP4 under the control of an inducible promoter and transfected into U937. The resultant cell line, DH42, was hygromycin resistant, contained **VDR** cDNA, expressed fewer **VDRs** than controls, and showed a substantial decrease in antiproliferative response to 1,25(OH)-2D-3. However, 1,25(OH)-2D-3 increased the number of cells expressing macrophage cell surface Ags, including [illegible] and [illegible]. A subpopulation of smaller cells did not express the differentiation markers after cadmium stimulation. Cell cycle analysis showed shifts in the distribution of cells from G1 to S phase, which were more pronounced after cadmium treatment. A considerable proportion of cells were outside the cycle and DNA fragmentation confirmed apoptosis. Thus, the functional outcome of the **VDR antisense** transfection suggests that in the myelomonocytic lineage, **VDR** expression may act as a protective mechanism against programmed cell death.

L9 ANSWER 1[illegible] OF [illegible] BIOSIS COPYRIGHT [illegible] BIOLOGICAL ABSTRACTS INC.DUPLICATE [illegible]

ACCESSION NUMBER: 199[illegible] BIOSIS
DOCUMENT NUMBER: PREV[illegible]
TITLE: Vitamin D receptor expression is required for growth modulation by 1-alpha,25-dihydroxyvitamin D-3 in the human prostatic carcinoma cell line ALVA-31.
AUTHOR(S): Hedlund, T. E.; [illegible], K. A.; Miller, [illegible]
CORPORATE SOURCE: [illegible] Dep. Pathol., Box [illegible], Univ. [illegible] Health Sci. Cent., 4[illegible] E. Ninth Ave., Denver, [illegible] USA
SOURCE: [illegible]
ISSN: [illegible].
DOCUMENT TYPE: Article
LANGUAGE: English
AB [illegible]

1-alpha,25-dihydroxyvitamin [illegible] regulates the growth and differentiation of several human EC cell lines. Both genomic and non-genomic signalling pathways for 1,25 (OH)2-D3 have been reported, although the mechanism of action in EC cells has not been defined. We have provide data supporting an action of the nuclear vitamin D receptor (VDR) in mediating the growth-inhibitory effects of 1,25 (OH)2-D3 in these cells. In the VDR-rich cell line AIJA-1, the addition of 1,25 (OH)2-D3 (10 nM) or the progestin R5020 (10 nM) for 48 h produced significant changes in VDR mRNA expression. In contrast, the cell line TERA-1, which lacks VDRs, failed to show any change in VDR mRNA expression after treatment with 1,25 (OH)2-D3. To investigate the role of the VDR in this system, transient transfection studies were performed. AIJA-1 cells were stably transfected with an antisense VDR cDNA construct in an attempt to reduce VDR expression. Antisense mRNA expression among clones was associated with: (a) reduced or abolished sensitivity to the growth effects of 1,25 (OH)2-D3, on growth; (b) decreased numbers of VDRs per cell, as measured by radioliganded-ligand binding; and (c) a lack of induction of the VDR-regulated enzyme 24-hydroxylase in response to 1,25 (OH)2-D3. From these studies we conclude that the antiproliferative effects of 1,25(OH)2 D3 require expression of the nuclear VDR in this system.

L9 ANSWER 11 OF 23 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 14

ACCESSION NUMBER: 1994:256969 BIOSIS
DOCUMENT NUMBER: PREV199447269269
TITLE: Identification of a vitamin D-responsive element in the 5'-flanking region of the rat 25-hydroxyvitamin D-3 24-hydroxylase gene.
AUTHOR: Ohyama, Yoshiko [1]; Noshiro, Makoto; Okuda, Kazuo; Okazaki, Toshiaki; Kato, Shigeaki; Suda, Tatsuo; Yamamoto, Osamu; Noshiro, Michihide; Kato, Yukio
CORPORATE SOURCE: [1] Graduate Dep. Gene Sci., Fac. Sci., Hiroshima Univ., 1-3-1 Kagamiyama, Higashi-Hiroshima 724 Japan.
SOURCE: Journal of Biological Chemistry, (1994) Vol. 269, No. 14, pp. 10545-10550.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The 5'-flanking region of the rat vitamin D-3 24-hydroxylase (P450c24) gene was examined and a vitamin D-responsive element (VDRE) responsible for the 1-alpha,25-dihydroxyvitamin D-3 [1,25-(OH)2-D3] enhancement was identified. Unidirectional deletion analyses of the 5'-flanking region indicated that the region (-191 to -112) is involved in vitamin D responsiveness. Further functional analyses showed that the segment (-164 to -127) conferred the hormone responsiveness in an orientation-independent manner when it was placed upstream of the heterologous thymidine kinase promoter of the rabbit beta-globin gene. The segment (-164 to -127) contained two direct repeat motifs (AGGTCA) which are the other VDREs found in the steroid/thyroid hormone receptor superfamily. Synthetic oligonucleotides containing the proximal VDRE were used in functional analyses and gel mobility shift assays. The proximal (-152 to -138) and the distal (-138 to -124) direct repeat sequences (AGGTCA) in response to 1,25-(OH)2-D3, the ligand for the vitamin D receptor. Furthermore, the proximal direct repeat sequence with the vitamin D receptor and a nuclear accessory factor(s) in HeLa cell nuclear extract in the presence of 1,25-(OH)2-D3. These results indicate that a direct repeat motif, AGGTCA, located at -152 to -138 plays a pivotal role in the vitamin D-mediated induction of the rat P450c24 gene expression.

L4 ANSWER 1 OF 1 MEDLINE [illegible]

ACCESSION NUMBER: [illegible]
DOCUMENT NUMBER: [illegible]
TITLE: [illegible] vitamin D receptor and calbindin-D28k mRNA levels in Alzheimer hippocampal CA1 neurons [illegible] with calbindin-28k mRNA levels.

AUTHOR: [illegible]

CORPORATE SOURCE: [illegible]

SOURCE: [illegible]
Journal code: [illegible]. ISSN: [illegible].

PUB. COUNTRY: [illegible]
DOCUMENT TYPE: [illegible]
LANGUAGE: [illegible]
FILE SEGMENT: [illegible]
ENTRY MONTH: [illegible]
ENTRY DATE: [illegible]

AB [illegible]

when the cells were incubated with the vitamin for 24 h before the FA treatment. 22-oxa-1,25 (OH)2D3 (OCT), an analog derivative of 1alpha25(OH)2D3, having high affinity for the vitamin D3 receptor **VDR**, also interfered with the FA-induced inhibition [illegible] c-fos gene expression in the TNF-alpha-treated cells. In contrast, this was [illegible] [illegible] [illegible]. Moreover, we observed that the interfering effect was clearly [illegible] by pretreatment with **VDR antisense** [illegible] 1alpha [illegible] interfered with FA inhibition [illegible] TRE-[illegible] binding activity of AP-1 in the [illegible]-treated cells. Furthermore, 1alpha [illegible] [illegible] the AP-1-[illegible] [illegible] [illegible] TNF-[illegible] in the [illegible]-treated cells. The present study suggests a regulatory interference by 1alpha25(OH)2D3 [illegible] FA inhibition of TNF-alpha-induced AP-1 activity in osteoblasts.

L9 ANSWER 14 OF 23 MEDLINE [illegible]

ACCESSION NUMBER: 2001[illegible] MEDLINE

DOCUMENT NUMBER: 21[illegible] PubMed ID: [illegible]

TITLE: 1alpha,25-dihydroxyvitamin D3 displays divergent growth effects in both normal and malignant cells.

AUTHOR: Rashid S F; Mountford J C; Gombart A F; Campbell M J

CORPORATE SOURCE: Division of Immunity & Infection, University of Birmingham Medical School, Queen Elizabeth Hospital, Edgbaston, B15 2TT, Birmingham, United Kingdom.

SOURCE: STEROIDS, (2001 Mar-May) 66 (3-5) 433-40. Journal code: [illegible]. ISSN: 0039-128X.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 2001[illegible]

ENTRY DATE: Entered STN: [illegible]
Last Updated on STN: [illegible]
Entered Medline: [illegible]

AB Induction of growth arrest and differentiation of some cancer cells by 1alpha,25-dihydroxyvitamin D(3) [1alpha,25(OH)(2)D(3)], and its potent analogs, is well characterized. However, aggressive cancer cell lines are often either insensitive to the antiproliferative effects of 1alpha,25(OH)(2)D(3) or require toxic concentrations to recapitulate them which has, to-date, precluded its use in anticancer therapy. Therefore we are interested in mechanisms by which 1alpha,25(OH)(2)D(3) signaling has become deregulated in malignant cells in order to identify novel therapeutic targets. We observed previously that 1alpha,25(OH)(2)D(3) and its metabolites, generated via the C-24 oxidation pathway, drive simultaneous differentiation and hyper-proliferation within the same cell population. Thus we have proposed that metabolism of 1alpha,25(OH)(2)D(3) via the C-24 oxidation pathway represents a novel-signaling pathway, which integrates proliferation with differentiation. In the current study we examined further the role of this pathway and demonstrated that these effects are not restricted to leukemic cells but are [illegible] also in both normal myeloid progenitors and breast cancer cell lines. Intriguingly, stable transfection of MCF-7 breast cancer cells with **antisense** vitamin D receptor (**VDR**) [illegible] antiproliferative sensitivity to 1alpha,25(OH)(2)D(3) but significantly enhanced growth stimulation, which, in turn, was [illegible] by inhibiting metabolism of 1alpha,25(OH)(2)D(3) via C-24 oxidation pathway with [illegible]. Taken together, these studies indicate that metabolism of 1alpha,25(OH)(2)D(3) via C-24 oxidation pathway gives rise to ligands with different [illegible] effects. We propose that this mechanism may allow the [illegible] population expansion and cell maturation during differentiation. [illegible] cells appear to corrupt this process during malignant transformation, by only responding to the pro-proliferative signals, thereby deriving a clonal advantage.

L9 ANSWER [illegible] MEDLINE DUPLICATE [illegible]
ACCESSION NUMBER: [illegible] MEDLINE
DOCUMENT NUMBER: [illegible] PubMed ID: [illegible]
TITLE: The anti-proliferative effects of 1alpha,25(OH)2D3 on breast and prostate cancer cells are associated with induction of BRCA1 gene expression.
AUTHOR: Campbell M J; Gombart A F; Kwok S H; Park S; Koeffler H P
CORPORATE SOURCE: Department of Medicine, Division of Medical Sciences, University of Birmingham, Clinical Research Institute, Queen Elizabeth Hospital, Edgbaston, Birmingham, B15 2TH, UK.
SOURCE: ONCOGENE, [illegible]
Journal code: [illegible] ISSN: [illegible]
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: [illegible]
ENTRY DATE: Entered STN: [illegible]
Last Updated on STN: [illegible]
Entered Medline: [illegible]

AB The anti-proliferative action of the seco-steroid hormone 1alpha, 25-dihydroxyvitamin D3 (1alpha,25(OH)2D3) extends to some, but not all breast and prostate cancer cell lines. By elucidating the molecular mechanisms mediating the sensitivity of these cells, we can identify critical target genes regulated directly or indirectly by 1alpha,25(OH)2D3 and pathways potentially disrupted during transformation. In this study, we demonstrated the induction of expression of BRCA1 mRNA and protein as well as transcriptional activation from the BRCA1-promoter by 1alpha,25(OH)2D3 in the sensitive breast cancer cell line MCF-7. This was not observed in the 1alpha,25(OH)2D3-resistant breast cancer cell line MDA-MB-436. The induction of BRCA1 mRNA was blocked by cyclohexamide. This indicated that transcriptional activation was mediated indirectly by the vitamin D receptor (**VDR**). Inhibition of **VDR** protein levels by stable transformation of the anti-sense **VDR** in MCF-7 reduced the sensitivity of MCF-7 to 1alpha,25(OH)2D3 by [illegible]-fold. In addition, the induction of BRCA1 protein and transcriptional activation of a BRCA1 promoter-[illegible] reporter [illegible] was [illegible] in the stable transformant with the greatest reduction of **VDR** levels. Examination of other breast and prostate cancer cell lines revealed that sensitivity to the anti-proliferative effects of 1alpha, 25(OH)2D3 was strongly associated with an ability to modulate BRCA1 protein. Furthermore, the expression of the estrogen receptor in these cell lines strongly correlated with their sensitivity to 1alpha,25(OH)2D3 and their ability to modulate BRCA1 expression. Taken together, our data support a model whereby the anti-proliferative effects of 1alpha,25(OH)2D3 are mediated, in part, by the induction of BRCA1 gene expression via transcriptional activation by factors induced by the **VDR** and that this pathway is disrupted during the development of prostate and breast cancers.

L9 ANSWER 16 OF 23 MEDLINE DUPLICATE 15
ACCESSION NUMBER: [illegible] MEDLINE
DOCUMENT NUMBER: [illegible] PubMed ID: [illegible]
TITLE: Gene expression, signal transduction and tissue-specific [illegible]
AUTHOR: [illegible]
CORPORATE SOURCE: [illegible]
SOURCE: [illegible]

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: [illegible]
ENTRY MONTH: [illegible]
ENTRY DATE: Entered STN: [illegible]
Last Updated on STN: [illegible]
Entered Medline: [illegible]

AB [illegible] extracellular matrix (ECM)-mediated biomineralization. The intent of this review is to evaluate the sequential timing and [illegible] information prerequisite for tissue-specific biomineralization. Recent investigations suggest that 1,25-dihydroxyvitamin D3 functions to up-regulate **VDR** (vitamin D receptor) that in turn could induce structural gene products, including calcium-binding proteins and several ECM proteins (e.g., enamelins, amelogenins, dentine sialoglycoproteins (DSP) and dentine phosphoproteins (DPP)), resulting in dentine and enamel formation. Inhibition of regulatory gene products and/or their receptors likely results in hypoplastic and/or hypomineralized ECM as a direct consequence of down-regulated (1) transcription and/or translation of structural and regulatory genes, (2) posttranslational modifications, (3) and/or decreased calcium transport to the forming dentine and enamel matrices. Advances in serumless in vitro culture methodology; computer-assisted access to nucleic acid sequences for probes to define when, where, and how many specific regulatory and structural gene products are expressed; **antisense** [illegible] to inhibit specific translation; and [illegible] techniques to analyze [illegible] mineralization [illegible] provide additional avenues to investigate tissue-specific biomineralization.

L9 ANSWER 17 OF 23 MEDLINE
ACCESSION NUMBER: 2001130658 MEDLINE
DOCUMENT NUMBER: 21124147 PubMed ID: 11149494
TITLE: 25-hydroxyvitamin D 1alpha-hydroxylase: structure of the mouse gene, chromosomal assignment, and developmental expression.
AUTHOR: Panda D K; Al Kawas S; Seldin M F; Hendy G N; Goltzman D
CORPORATE SOURCE: Calcium Research Laboratory, Royal Victoria Hospital, Montreal, Quebec, Canada.
SOURCE: JOURNAL OF BONE AND MINERAL RESEARCH, (2001 Jan) 16 (1) 46-56.
Journal code: [illegible]. ISSN: 0884-0431.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF[illegible]
ENTRY MONTH: [illegible]
ENTRY DATE: Entered STN: [illegible]
Last Updated on STN: [illegible]
Entered Medline: [illegible]

AB The murine homologue of the 25-hydroxyvitamin D [illegible] 1alpha-hydroxylase gene (1alpha(OH)ase; Cyp27b1), which is mutated in humans with vitamin D-dependent rickets type 1 (VDDR-I; also known as pseudovitamin D-deficiency rickets [PDDR]) was cloned and characterized. Like the human, the mouse gene has nine exons, and the exon-intron organization is well conserved. By interspecific backcross analysis, the Cyp27b1 gene was mapped to [illegible] on mouse Chr 10. This is in a region syntenic with human Chr 12q13.1-q13.3 to which the human 1alpha(OH)ase gene was previously mapped. Kidney expression of the 1alpha(OH)ase was localized to proximal tubules and was higher in the adult mouse than in the fetus, consistent with the increased role of [illegible]

circulating hormone postnatally. Prenatally, the 1alpha OHase gene, together with the vitamin D receptor (VDR) gene, was expressed in embryonic stem cells, and expression of 1alpha OHase in bone and intestine was higher in the fetus than in the adult. These observations suggest that 1,25-dihydroxyvitamin D (1,25(OH)2D) plays a role in fetal development. In view of the fact that humans lacking 1alpha OHase have apparently normal prenatal development, this may point to functional redundancy in the fetal vitamin D system, which now can be explored further in mouse models in which the 1alpha OHase gene has been deleted.

L4 ANSWER 13 OF 18 CAPLUS COPYRIGHT [illegible] ACS
ACCESSION NUMBER: [illegible] CAPLUS
DOCUMENT NUMBER: [illegible]
TITLE: Accessing Single Nucleotide Polymorphisms in Genomic DNA by Direct Multiplex Polymerase Chain Reaction Amplification on Oligonucleotide Microarrays
AUTHOR(S): Huber, Martin; Muendlein, Axel; Dornstauder, Eva; Schneeberger, Christian; Tempfer, Clemens B.; Mueller, Manfred W.; Schmidt, Wolfgang M.
CORPORATE SOURCE: VBC-GENOMICS Bioscience Research GmbH, Vienna, 1030, Austria
SOURCE: Analytical Biochemistry (2002), 303(1), 25-33
CODEN: ANBCA2; ISSN: 0003-2697
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study introduces a DNA microarray-based genotyping system for accessing single nucleotide polymorphisms (SNPs) directly from a genomic DNA sample. The described one-step approach combines multiplex amplification and allele-specific solid-phase PCR into an on-chip reaction platform. The multiplex amplification of genomic DNA and the genotyping reaction are both performed directly on the microarray in a single reaction. Oligonucleotides that interrogate single nucleotide positions within multiple genomic regions of interest are covalently tethered to a glass chip, allowing quick anal. of reaction products by fluorescence scanning. Due to a fourfold SNP detection approach employing simultaneous probing of sense and antisense strand information, genotypes can be automatically assigned and validated using a simple computer algorithm. We used the described procedure for parallel genotyping of 10 different polymorphisms in a single reaction and successfully analyzed more than 100 human DNA samples. More than 99% of genotype data were in agreement with data obtained in control expts. with allele-specific oligonucleotide hybridization and capillary sequencing. Our results suggest that this approach might constitute a powerful tool for the anal. of genetic variation.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 18 CAPLUS COPYRIGHT [illegible] ACS
ACCESSION NUMBER: [illegible] CAPLUS
DOCUMENT NUMBER: [illegible]
TITLE: [illegible] VDR [illegible]
AUTHOR(S): [illegible]
CORPORATE SOURCE: Department of Pathophysiology, Second Military Medical University, Shanghai, [illegible]
SOURCE: [illegible]
CODEN: [illegible]; ISSN: [illegible]
PUBLISHER: [illegible]
DOCUMENT TYPE: Journal
LANGUAGE: [illegible]
AB [illegible] VDR [illegible] 1,25-dihydroxyvitamin D3 (1,25(OH)2D3) [illegible]

[illegible] cell line HOS-[illegible] was established. VDR mRNA and protein expression in HOS-[illegible] cells were determined by reverse transcription-polymerase chain reaction, RT-PCR and immunoblot, respectively, and its function was detected by transient transfection of a reporter gene (pBG-TK-CAT) with VDR. The effect of 1,25-(OH)2D3 on proliferation of HOS-[illegible] cells and induction of p21 mRNA, one of the VDR target genes, after blockade of VDR in the cells was studied by using cell VDRas1 stably expressing VDR **antisense** mRNA. The VDR as a hormone-dependent transcriptional factor was expressed in HOS-[illegible] cells. The inhibitory effects of 1,25-(OH)2D3 on the proliferation of HOS-[illegible] cells and induction of p21 gene expression were remarkably altered by blockade of VDR in the cells. The results showed that the effects of 1,25-(OH)2D3 on the proliferation of human osteosarcoma cell line HOS-[illegible] were mediated by the nuclear receptor VDR.

L9 ANSWER 2 OF 23 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: [illegible] CAPLUS
DOCUMENT NUMBER: [illegible]
TITLE: Establishing a human osteosarcoma cell line of stably-transfected vitamin D receptor **antisense** cDNA
AUTHOR(S): Chen, Yuxia; Liu, Yujian; Song, Lianqnian
CORPORATE SOURCE: Department of Pathophysiology, Department of Basic Medicine, Second Military Medical University, Shanghai, 200433, Peop. Rep. China
SOURCE: Di-Er Junyi Daxue Xuebao (2001), 22(3), 242-244
CODEN: DJXUE6; ISSN: 0258-879X
PUBLISHER: Di-Er Junyi Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB A human osteosarcoma cell line stably-transfected with human vitamin D receptor (VDR) **antisense** cDNA was established. The eukaryotic expression vector containing VDR **antisense** cDNA was constructed, and transferred into the human osteosarcoma cell line HOS-[illegible] by lipofectamine method. The stable transfectants were screened by G418, and the expression of exogenous VDR was further detected at protein level by immunohistochem. anal. The transcriptional activity mediated by VDR in the VDRas1 cells was detected at reporter gene level by transient transfection method. Six subclones (VDRas1-6) were isolated, and the level of endogenous VDR expression in the VDRas1 cells decreased significantly compared with that in the control cells. The transcriptional activity of the reporter gene CAT in the control cells increased by 3.5-fold when treated with 1 × 10-8 M 1,25-(OH)2D3 for 72 h, but the transcription of CAT in the VDRas1 cells could not be induced by 1,25-(OH)2D3. A cell line stably expressing VDR **antisense** cDNA is established for the further study of the mol. mechanisms of 1,25-(OH)2D3 effect and its analogs on proliferation and differentiation of the human osteosarcoma cell line.

L9 ANSWER 21 OF 23 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: [illegible] CAPLUS
DOCUMENT NUMBER: [illegible]
TITLE: [illegible]
INVENTOR(S): [illegible]
PATENT ASSIGNEE(S): [illegible]
SOURCE: [illegible]
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
W[illegible]	A1	[illegible]	W[illegible]	[illegible]

W: [illegible]
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
EP [illegible] A1 [illegible] EP [illegible]
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY

PRIORITY APPLN. INFO.: US [illegible] A [illegible]
W[illegible] W [illegible]

AB This invention pertains to the discovery that an amplification of the CYP24 gene or an increase in CYP24 activity is a marker for the presence of, progression of, or predisposition to, a cancer (e.g., breast cancer). Using this information, this invention provides methods of detecting a predisposition to cancer in an animal. The methods involve (i) providing a biol. sample from an animal (e.g. a human patient); (ii) detecting the level of CYP24 within the biol. sample; and (iii) comparing the level of CYP24 with a level of CYP24 in a control sample taken from a normal, cancer-free tissue where an increased level of CYP24 in the biol. sample compared to the level of CYP24 in the control sample indicates the presence of said cancer in said animal.

REFERENCE COUNT: [illegible] THERE ARE [illegible] CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L[illegible] ANSWER [illegible] OF [illegible] CAPLUS COPYRIGHT [illegible] ACS
ACCESSION NUMBER: 1998:338116 CAPLUS
DOCUMENT NUMBER: 129:1294[illegible]
TITLE: Method of treating Kaposi's sarcoma by vitamin-D receptor agonists
INVENTOR(S): Gill, Parkash S.
PATENT ASSIGNEE(S): Gill, Parkash S., USA
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
W[illegible]	A1	[illegible]	W[illegible]	[illegible]

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
AU [illegible] A1 [illegible] AU [illegible] [illegible]

PRIORITY APPLN. INFO.: US [illegible] P [illegible]
WO [illegible] W [illegible]

AP A novel and effective method for treating Kaposi's sarcoma (KS) in patients, by administration of an effective amt. of vitamin-D receptor (VDR) agonist. VDR agonists are capable of inhibiting the growth of KS cells in culture by suppressing the levels of [illegible] growth factors, IL-6 and IL-8, in KS cells. The VDR agonists may be administered to KS patients topically, orally, or parenterally. Substantive improvement in KS lesions is expected by [illegible] treatment with an [illegible] VDR agonist [illegible] [illegible]

By combination therapy with **VDR** agonists and IL-1, IL-6, and IL-8 inhibitors. Pharmaceutical compns. contg. the **VDR** agonists are also claimed.

L3 ANSWER 13 OF 13 CAPLUS COPYRIGHT
ACCESSION NUMBER: 97:[illegible] CAPLUS
DOCUMENT NUMBER: 97[illegible]
TITLE: Suppression of the 25-hydroxyvitamin D3 24-hydroxylase gene expression by the human TR4 orphan receptor, a member of steroid receptor superfamily (Meeting Abstract)
AUTHOR: [illegible]
CORPORATE SOURCE: [illegible]
SOURCE: [illegible]
DOCUMENT TYPE: MEETING ABSTRACT
LANGUAGE: English
FILE SEGMENT: Institute for Cell and Developmental Biology
ENTRY MONTH: 199[illegible]
ENTRY DATE: Entered STN: 1996[illegible]
Last Updated on STN: 1996[illegible]

AB Human TR4 orphan was demonstrated to repress the retinoid signal pathway by occupancy of the response element for RAR and RXR with higher affinity compared with the RAR/RXR heterodimer. Here we demonstrate that human TR4 orphan receptor specifically binds to AGGTCA direct repeats spaced by 4 nucleotides (DR4), a response element for vitamin D receptor (**VDR**). In addition, in transient transfection, we found TR4 orphan receptor suppresses rat 25-hydroxyvitamin D3 24-hydroxylase gene promoter activity which contains nature response element for vitamin D receptor. This suppression is dose and **VDR** response element dependent. The **antisense** staining of 16.5-day mouse embryos showed that TR4 orphan receptor can co-localize with **VDR** in mouse kidney and intestine, which further suggested the idea that TR4 orphan receptor may be involved in the regulation of vitamin D system, a system that plays in the proliferation and differentiation of bone cells.

L1 ANSWER 1 OF 1 MARPAT COPYRIGHT ACS
ACCESSION NUMBER:
DOCUMENT NUMBER:
TITLE:
INVENTOR(S):
PATENT ASSIGNEE(S):
SOURCE:
DOCUMENT TYPE:
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000068180	A1	20001116	WO	
W: CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1185490	A1	20020313	EP	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				

PRIORITY APPLN. INFO.:

AB This invention pertains to the discovery that an amplification of the CYP24 gene or an increase in CYP24 activity is a marker for the presence of, progression of, or predisposition to, a cancer (e.g., breast cancer). Using this information, this invention provides methods of detecting a predisposition to cancer in an animal. The methods involve (i) providing a biol. sample from an animal (e.g. a human patient); (ii) detecting the level of CYP24 within the biol. sample; and (iii) comparing the level of CYP24 with a level of CYP24 in a control sample taken from a normal, cancer-free tissue where an increased level of CYP24 in the biol. sample compared to the level of CYP24 in the control sample indicates the presence of said cancer in said animal.

REFERENCE COUNT: THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 1 OF 4 BIOSIS COPYRIGHT [illegible] BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: [illegible] BIOSIS

DOCUMENT NUMBER: PREV[illegible]

TITLE: **Ribozyme-**[illegible] **vitamin D receptor** [illegible] activity in cell culture.

AUTHOR(S): [illegible], A. F.; [illegible], D.; [illegible], H. P.

CORPORATE SOURCE: Div. Hematol./Oncol., Cedars-Sinai Med. Center, UCLA [illegible] Med., Div. Nutrition, Los Angeles, CA USA

SOURCE: Blood, [illegible], Vol. [illegible], No. [illegible] SUPPL. 1, pp. [illegible].
Meeting Info.: Abstracts Submitted to the [illegible] Annual Meeting of the American Society of Hematology [illegible], [illegible], USA [illegible]
ISSN: [illegible]

DOCUMENT TYPE: Conference

LANGUAGE: English

L14 ANSWER [illegible] OF 4 CAPLUS COPYRIGHT [illegible] ACS

ACCESSION NUMBER: [illegible] CAPLUS

DOCUMENT NUMBER: [illegible]

TITLE: Construction of lentiviral vectors for inducible high level controlled expression of transferred genes in mammalian cells and therapeutical uses

INVENTOR(S): Evans, Ronald M.; Saez, Enrique; Verma, Inder M.

PATENT ASSIGNEE(S): The Salk Institute for Biological Studies, USA

SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
[illegible]	A[illegible]	[illegible]	WO [illegible]	[illegible]

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, [illegible], [illegible], [illegible], [illegible], [illegible], [illegible], [illegible], [illegible], [illegible], [illegible], [illegible], [illegible], [illegible], [illegible], [illegible], [illegible], [illegible], [illegible], GM, HR, HU, [illegible], [illegible], IN, [illegible], [illegible], KE, KG, KP, KR, KZ, [illegible], LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, [illegible], PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, [illegible], AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, [illegible], AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US [illegible]

AB The present invention provides inducible gene transfer systems and gene transfer vectors of lentivirus for the safe and effective transfer and expression of genes in mammalian cells, and for a very high level of control of expression of the transferred genes. The inducible gene transfer systems of the present invention may be lentiviral vectors comprising a self-inactivating [illegible] LTR, a modulator-responsive promoter, a nuclear import signal, a promoter operatively associated with [illegible] [illegible] a modulator-responsive receptor, an RNA stabilizing [illegible], and a self-inactivating [illegible] LTR. [illegible]

L14 ANSWER 3 OF 4 CAPLUS COPYRIGHT [illegible] ACS

ACCESSION NUMBER: [illegible] CAPLUS

DOCUMENT NUMBER: [illegible]

TITLE: [illegible]

[illegible] presence [illegible] progression [illegible] predisposition [illegible] cancer

INVENTOR(S): [illegible]

PATENT ASSIGNEE(S): [illegible] of the University of California, USA

SOURCE: PCT Int. Appl., [illegible] pp.
CODEN: [illegible]

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO [illegible]	A1	[illegible]	WO [illegible]-US[illegible]	[illegible]
W: CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 125[illegible]	A1	20021113	EP 2000-[illegible]	[illegible]
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				

PRIORITY APPLN. INFO.: US 1999-2[illegible] A 1999[illegible]
WO 2000-US[illegible] W 20[illegible]

AB This invention pertains to the discovery that an amplification of the CYP24 gene or an increase in CYP24 activity is a marker for the presence of, progression of, or predisposition to, a cancer (e.g., breast cancer). Using this information, this invention provides methods of detecting a predisposition to cancer in an animal. The methods involve (i) providing a biol. sample from an animal (e.g. a human patient); (ii) detecting the level of CYP24 within the biol. sample; and (iii) comparing the level of CYP24 with a level of CYP24 in a control sample taken from a normal, cancer-free tissue where an increased level of CYP24 in the biol. sample compared to the level of CYP24 in the control sample indicates the presence of said cancer in said animal.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:161479 CAPLUS

DOCUMENT NUMBER: 132:204016

TITLE: Adenoviral vectors and inducible expression system for gene expression and therapy

INVENTOR(S): Mehtali, Majid; Sorg-guss, Tania

PATENT ASSIGNEE(S): Transgene S.A., Fr.

SOURCE: PCT Int. Appl., [illegible] pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000012741	A2	2000[illegible]	WO 1999-FR[illegible]	199[illegible]
WO 2000012741	A3	2000[illegible]		
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR [illegible]	A1	[illegible]	FR 1998-[illegible]	[illegible]
CA [illegible]	AA	[illegible]	CA 1999-[illegible]	[illegible]
AU [illegible]	A1	[illegible]	AU 1999-[illegible]	[illegible]
EP [illegible]	A2	[illegible]	EP 1999-[illegible]	[illegible]
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

ACCESSION NUMBER:
DOCUMENT NUMBER:
TITLE: [illegible] 1,25-dihydroxyvitamin D3-mediated transcriptional activation

AUTHOR(S):

CORPORATE SOURCE:
SOURCE:
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The gene for rat bone gla protein, BGP, was isolated and 1,650 base pairs (bp), including 1150 bp of 5' flanking DNA, were placed up-stream of the human GH reporter gene. After transient transfection into the osteoblast-like rat osteosarcoma cell line ROS 17/2.8, the BGH primer demonstrated a low level of basal activity that was increased approx. 17-fold by the addn. of 10-8 M 1,25-dihydroxyvitamin D3 [1,25-(OH)2D3]. A single 200-bp fragment (-426 to -274) was sufficient to confer hormone inducibility upon both heterologous and homologous promoters. Deletion studies, complemented by evaluation with synthetic oligomers, enabled localization of the 1,25-(OH)2D3 response element to within 142 bp (-184 to -43), which contains an element with an imperfect direct repeat (TGTTCA NG TGTTCA) and homol. to other steroid-responsive elements. Gel retardation assays demonstrated that partially purified chick intestinal 1,25-(OH)2D3 receptor bound specifically and with high affinity to a DNA fragment contg. the putative 1,25-(OH)2D3 response element, and this binding was perturbed by monoclonal antibodies to the 1,25-(OH)2D3 receptor. Surprisingly, the 250-bp fragment, when linked in an **antisense** orientation with respect to the BGP promoter, blocked basal and hormone-dependent gene expression. However, a 146-bp fragment 5' to the 184-bp element (-330 to -184) restored 3-fold inducibility when linked to the first fragment in the same orientation, suggesting the cooperativity between at least two elements to achieve the normal regulation obsd. in this gene.